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ONE HUNDRED FIFTEENTH CONGRESS

Congress of the United States

House of Representatives

COMMITTEE ON ENERGY AND COMMERCE
2125 RAYBURN HOUSE OFFICE BUILDING
WASHINGTON, DC 20515-6115

Majority (202) 225-2927
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MEMORANDUM

March 1, 2017

To: Subcommittee on Health Democratic Members and Staff

Fr: Committee on Energy and Commerce Democratic Staff

Re: Hearing on "Examining FDA's Generic Drug and Biosimilar User Fee Programs."

On **Thursday, March 2nd, at 10:00 a.m., in room 2123 of the Rayburn House Office Building**, the subcommittee will hold a hearing on the reauthorization of the generic drug and biosimilar user fee agreements.

I. GENERIC DRUG USER FEE (GDUFA)

A. Background

The Generic Drug User Fee Amendments of 2012 (GDUFA, or GDUFA I) was signed into law as part of the Food and Drug Administration Safety and Innovation Act (FDASIA) in response to the overwhelming number of pending generic drug applications, or abbreviated new drug applications (ANDAs), at the Food and Drug Administration (FDA). This backlog of applications led FDA and industry to establish a user fee program to ensure the timely review of ANDAs and expedite access to generics. Under GDUFA I, FDA was to collect $299 million annually over five years, adjusted for inflation and workload, based on the projection that FDA would receive 750 ANDAs per year.

B. GDUFA II Reauthorization

Over the first four years of GDUFA I, FDA received on average approximately 1,000 annual applications exceeding the program's initial projections. To address the higher than expected workload and to institute program enhancements to improve program predictability and

effectiveness, industry and FDA agreed to user fees totaling $493.6 million annually, adjusted each year for inflation, in GDUFA II.[1]

1. User Fees

There are two major modifications to the GDUFA I user fee structure under GDUFA II. First, annual program fees will replace individual application fees for sponsors with one or more approved ANDAs. This will improve predictability of the fee base and will better align sponsor fees with program costs. This annual fee schedule will be divided across three tiers: Large (companies with 20 or more approved ANDAs), Medium (companies with 6-19 approved ANDAs), and Small (companies with 5 or fewer approved ANDAs). Finished Dosage Form (FDF) and Active Pharmaceutical Ingredient (API) facilities will continue to pay annual fees as agreed upon in GDUFA I. Second, the Prior Approval Supplement (PAS) fee will be eliminated. Yearly total PAS fees are difficult to accurately project because PAS submissions are unpredictable. Furthermore, collecting these fees required administrative resources. Industry and FDA agreed the PAS fee should be eliminated and encompassed in the new ANDA fee program.[2]

2. ANDA Review Goals

GDUFA II also establishes simplified review goals for ANDAs. FDA will review and act on 90 percent of standard generic applications within ten months after the date of submission, or within eight months for priority applications. An action can mean either an approval, refuse-to-receive, complete response, withdrawal or denial. Priority status will be provided by FDA for submissions identified as eligible for expedited review. This currently includes applications for drugs in shortage, first generics, sole source generics, or drugs that meet a public health need. FDA has also committed in GDUFA II to increasing communication with sponsors of complex products through an optional pre-ANDA submission process to provide sponsors with greater clarity around regulatory expectations earlier in order to assist with the development of complete submissions. GDUFA II also increases transparency and communication between the agency and applicants during the review process through use of Information Requests (IRs) and Division Review Letters (DRLs). These communications will detail any deficiencies about an application to a sponsor around the midpoint of the review cycle so as to help decrease the number of review cycles.

FDA and industry also agreed to several accommodations for small business. After convening with small businesses as part of a working group, FDA has agreed to three distinct considerations. First, a facility or ANDA sponsor will only be charged an annual fee if the ANDA in which it is listed is approved. Previously, a facility would pay an annual fee regardless of whether it was listed in any approved ANDAs. This led to facilities being charged even

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[1] U.S. Food and Drug Administration (FDA), *Background for the Proposed Changes for Reauthorization of GDUFA In Fiscal Years 2018 Through 2022*.

[2] FDA, *GDUFA II Fee Structure Summary* (https://www.fda.gov/downloads/ForIndustry/UserFees/GenericDrugUserFees/UCM525236.pdf FDA).

though they may have no generic drug revenue stream. Second, small businesses will be included in the GDUFA II annual program fee structure. Third, Contract Manufacturing Organizations (CMOs) will be responsible for one-third of the annual fee paid by firms that manufacture under ANDAs which they or their affiliates own.[3]

C. Addressing the ANDA Backlog

During GDUFA I, ANDA review goals were complex and difficult to operationalize. While it allowed FDA to organize workload and make more headway, the review goals still led to large gaps between negotiated goals and stakeholder expectations. Despite these difficulties, FDA met its goal by acting on 90 percent of the pre-GDUFA I backlog. Further, FDA has assigned a target action date (TAD) to ensure action on all applications in the pre-GDUFA I backlog by the end of 2017. All TADs will be converted to goal dates under GDUFA II, with FDA committed to reviewing and acting within the metrics of GDUFA II.

II. BIOSIMILAR USER FEE ACT (BSUFA)

A. Background

Given the inherent differences between biologic products and traditional medicines, a separate regulatory pathway was created to approve new biologics that are similar to existing biologic products under the Biologics Price Competition and Innovation Act (BPCIA).[4] In order to be FDA approved, a biosimilar is required to have the same mechanism of action, route of administration, dosage, form, and strength of another biologic product.[5] In addition, it must match and can only be utilized to treat already approved conditions or indications. Of note, there is an additional FDA classification for "interchangeable biologic products."[6]

B. Overview of Biosimilars User Fee Act (BsUFA)

BPCIA also directed FDA to develop recommendations for a biosimilar user fee program for fiscal years 2013 through 2017 in consultation with Congress, industry, scientific and academic experts, health care professionals, and patient and consumer advocates. The first Biosimilar User Fee Act (BsUFA) was enacted as part of the FDASIA in 2012. Like other user fee programs, the fees collected by the agency are used to support the review of marketing

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[3] *See* Note 1.

[4] Patient Protection and Affordable Care Act, Public Law No. 111-148, See *Title VII Subtitle A – Biologics Price Competition and Innovation* (https://www.ssa.gov/OP_Home/comp2/F111-148.html).

[5] *Id.*

[6] FDA, *Information for Industry (Biosimilars)* (Aug. 27, 2015) (https://www.fda.gov/Drugs/DevelopmentApprovalProcess/HowDrugsareDevelopedandApproved/ApprovalApplications/TherapeuticBiologicApplications/Biosimilars/ucm241720.htm).

applications for biosimilar biological products and are meant to supplement funding appropriated by Congress. Fees collected under BsUFA include fees for biosimilar product development (BPD), marketing applications, supplements, manufacturing establishments, and products.

BsUFA performance goals[7] included targets for FDA to review 70 percent of applications for biosimilars within 10 months of receipt in fiscal years 2013 and 2014, 80 percent in fiscal year 2015, 85 percent in fiscal year 2016, and 90 percent in fiscal year 2017. Program development activities funded through biosimilar user fees include: biosimilar biological product development meetings; investigational new drug applications (INDs); development of the scientific, regulatory, and policy infrastructure necessary for review of biosimilar applications; and development of standards for biological products subject to review and evaluation. Other activities funded through the biosimilar user fees include: review of advertising and labeling prior to approval of a biosimilar; review of required post-marketing studies; and inspection of biosimilar establishments.

C. Biosimilar User Fee Act Reauthorization (BsUFA II)

At the time of BsUFA I, the U.S biosimilar industry was just beginning to form. Predicting the volume of applications and total revenue from application fees was difficult. In BsUFA II it is proposed that an annual BsUFA program fee will be assessed for each product approved as of October 1. BsUFA II will retain the initial, annual, and reactivation biosimilar biological product development (BPD) fees while removing the supplement fee and establishment fee. Sponsors will be limited to five BsUFA Program fees for a fiscal year application. There will be a modification to the budget authority spending trigger, which will be met in a fiscal year if the costs funded by budget authority are not more than 15 percent below the inflation adjusted amount for that year. It is estimated FDA will need approximately $45 million to cover program costs in fiscal year (FY) 2018. In order to improve predictability for sponsors, BsUFA fees cannot initially increase more than 25 percent from FY 2018 amounts. In addition to the review of biosimilars, user fees provided under BsUFA II will also be used to strengthen staff capacity, draft guidance related to biosimilar development, and provide for improvements in the scheduling and format of meetings between FDA and industry.

BsUFA II will also establish an application review model that strives to result in more first-cycle approvals. It is similar to the review model prescribed in the Prescription Drug User Fee Act (PDUFA). The BsUFA II review model will add FDA-sponsor communication requirements as well as performance goals for review (10-month review). In order to address the increasing number of meeting requests from sponsors, BsUFA II provides additional flexibility for FDA in meeting format and institutes new timelines for meeting scheduling. Biosimilar Initial Advisory meetings, which are general discussion on a proposed product and its qualifications as a biosimilar, will occur within 75 calendar days from receipt of meeting request

[7] FDA, *Biosimilar Biological Product 2 Authorization Performance Goals and 3 Procedures Fiscal Years 2013 through 4 2017* (https://www.fda.gov/downloads/Drugs/DevelopmentApprovalProcess/HowDrugsareDevelopedandApproved/ApprovalApplications/TherapeuticBiologicApplications/Biosimilars/UCM281991.pdf).

rather than 90 days. Biosimilar Biological Product Development (BPD) Type 2 meetings, which focus on a specific issue or questions related to an ongoing BPD program, will take place within 90 days of receipt of a meeting request rather than 75 calendar days. Enhancements in FDA workforce are included to assist with the workload.

D. H.R. 749, Lower Drug Costs Through Competition Act

The hearing will also focus in part on H.R. 749, the Lower Drug Costs Through Competition Act, introduced by Rep. Schrader (D-OR) and Rep. Bilirakis (R-FL). The bill aims to incentivize generic competition. H.R. 749 establishes the priority review of six months for generic drug applications for which there is no comparable generic drug on the market or there is a drug shortage, creates a priority review voucher (PRV) for generic drug manufacturers that receive approval and market a generic drug where there is no comparable generic drug or there is a drug shortage, strives to close the loophole in the Tropical Disease Priority Review program that allows manufacturers to receive a PRV for drugs that have been previously approved, and requires reporting on the number of applications that were filed for generic drug review, the average and median time applications for generic drugs have been pending, the number of generic drug applications certified to not violate valid patent, and the number of generic drug applications subject to priority review.

In addition, the legislation would require a study by the Government Accountability Office (GAO) to review the implementation and effectiveness of the Risk Evaluation and Mitigation Strategies (REMS) program and the impact of REMS programs on generic entry. There is evidence that some drug manufacturers have been using REMS programs as a way to block or impede generic entry.

III. WITNESSES

Panel I:

Janet Woodcock, M.D.
Director, Center for Drug Evaluation and Research
U.S. Food and Drug Administration

Panel II:

David Gaugh
Senior Vice President of Sciences and Regulatory Sciences
Association for Accessible Medicines

Bruce A. Leicher
Senior Vice President and General Counsel
Momenta Pharmaceuticals, Inc.
Chair, The Biosimilars Council, a Division of the Association for Accessible Medicines

Juliana Reed
Vice President of Government Affairs
Coherus BioSciences
Immediate Past President, The Biosimilars Forum

Kay Holcombe
Senior Vice President of Science Policy
Biotechnology Industry Organization

Allan Coukell
Senior Director, Health Programs
The Pew Charitable Trusts